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  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


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L2             1 SEA FILE=REGISTRY S(W)LANSOPRAZOLE
L3            28 SEA FILE=CAPLUS L2


=> d l3 1-28 ibib abs hit

L3   ANSWER 1 OF 28  CAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:         2003:261832  CAPLUS
DOCUMENT NUMBER:          138:287676
TITLE:                    Preparation of benzimidazole derivatives as ulcer and
                          gastric acid secretion inhibitors
INVENTOR(S):              Kamiyama, Keiji; Sato, Fumihiko; Banno, Hiroshi;
                          Hasuoka, Atsushi
PATENT ASSIGNEE(S):       Takeda Chemical Industries, Ltd., Japan
SOURCE:                   PCT Int. Appl., 111 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 Japanese
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.   DATE
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     WO 2003027098      A1   20030403       WO 2002-JP9746    20020924
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS,
             LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,
             PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,
             UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
             TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
             CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
             NE, SN, TD, TG
     JP 2003313186      A2   20031106       JP 2002-277780    20020924
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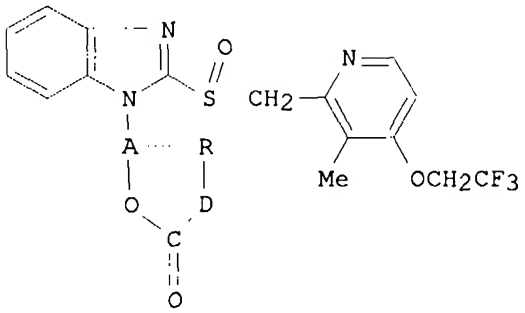
PRIORITY APPLN. INFO.: JP 2001-292619 A 20010925
JP 2002-47204 A 20020222
OTHER SOURCE(S): MARPAT 138:287676
GI



I

AB The title compds. I [A = (un)substituted alkylidene; R = (un)substituted hydrocarbon, etc.; or A and R may together form a ring; D = O, etc.], useful as ulcer and gastric acid secretion inhibitors (no data), are prepd. I are prodrugs of 2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methyl]sulfinyl]-1H-benzimidazole and are said to show excellent stability to acids. I are said to show excellent in vivo activities such as antiulcer activity, gastric hydrochloric acid secretion inhibitory activity, mucosal protective activity, and anti-helicobacter pylori activity.

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT 64-17-5, Ethanol, reactions 67-63-0, 2-Propanol, reactions 74-88-4, Iodomethane, reactions 75-36-5, Acetyl chloride 79-30-1, Isobutyryl chloride 87-91-2, Diethyl (+)-tartrate 96-41-3, Cyclopentanol 100-51-6, Benzyl alcohol, reactions 109-86-4, 2-Methoxyethanol 123-38-6, Propionaldehyde, reactions 123-63-7, Paraldehyde 142-26-7, N-Acetylethanolamine 623-69-8, 1,3-Dimethoxy-2-propanol 2081-44-9, 4-Hydroxytetrahydropyran 2719-27-9, Cyclohexanecarbonyl chloride 3282-30-2, Trimethylacetyl chloride 3967-54-2, 4-Chloro-1,3-dioxolan-2-one 4043-59-8, 1,3-Diethoxy-2-propanol 4524-93-0, Cyclopentanecarbonyl chloride 4767-03-7, 2,2-Bis(hydroxymethyl)propanoic acid 5464-28-8, Glycerol formal 5819-19-2, 1-Chloroethyl benzoate 7681-82-5, Sodium iodide, reactions 32328-03-3, Diethyl 3-hydroxyglutarate 38870-89-2, Methoxyacetyl chloride 50893-53-3, 1-Chloroethyl chloroformate 84674-32-8, 1-Chloroethyl 2-methylpropanoate 98298-66-9, 1-Chloroethyl isopropyl carbonate 99464-83-2, 1-Chloroethyl cyclohexyl carbonate 103577-40-8 103577-45-3 **138530-95-7** 398135-98-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of benzimidazole derivs. as ulcer and gastric acid secretion inhibitors)

L3 ANSWER 2 OF 28 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:212906 CAPLUS
DOCUMENT NUMBER: 138:205056
TITLE: Preparation of optically pure lansoprazole
INVENTOR(S): Deng, Jingen; Peng, Xiaohua; Cui, Xin; Fu, Fangmin; Zhu, Jin; Chi, Yongxiang; Jiang, Yaozhong
PATENT ASSIGNEE(S): Chengdu Inst. of Organic Chemistry, Chinese Academy of Sciences, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 20 pp.
CODEN: CNXXEV

DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1329003	A	20020102	CN 2000-113036	20000619
CN 1117747	B	20030813		

PRIORITY APPLN. INFO.: CN 2000-113036 20000619
OTHER SOURCE(S): CASREACT 138:205056

AB Lansoprazole is optically resolved by allowing to react with chiral binaphthol (at a molar ratio of 1:2-6) in org. solvent for 12-72 h, standing at 10-30.degree. for 5-48 h, filtering to inclusion compd. with one optical configuration, sepg. lansoprazole and binaphthol from the inclusion compd. on chromatog. column to obtain oily or syrup lansoprazole; treating with 1-10% inorg. base soln. at 50-120.degree. for 5 min-2 h to pH 10-13 to obtain colorless or light yellow lansoprazole soln.; cooling in ice-salt bath for 1-3 h and at -20 to 10.degree. for 5-20 h to obtain white amorphous solid of lansoprazole; and recrystg. to obtain white crystal of lansoprazole.

IT 138530-94-6P, (+)-Lansoprazole **138530-95-7P**, (S)-Lansoprazole
RL: IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of optically pure lansoprazole)

L3 ANSWER 3 OF 28 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:662644 CAPLUS
DOCUMENT NUMBER: 138:214821
TITLE: Enantioselective disposition of lansoprazole in extensive and poor metabolizers of CYP2C19
AUTHOR(S): Kim, Kyoung-Ah; Shon, Ji-Hong; Park, Ji-Young; Yoon, Young-Ran; Kim, Min-Jung; Yun, Doo-Hee; Kim, Moon-Kyung; Cha, In-June; Hyun, Myung-Ho; Shin, Jae-Gook
CORPORATE SOURCE: Department of Pharmacology, Inje University College of Medicine and Clinical Pharmacology Center, Pusan Paik Hospital, Pusan National University, Pusan, S. Korea
SOURCE: Clinical Pharmacology & Therapeutics (St. Louis, MO, United States) (2002), 72(1), 90-99
CODEN: CLPTAT; ISSN: 0009-9236
PUBLISHER: Mosby, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The objective was to evaluate the enantioselective disposition of lansoprazole in relation to the genetic polymorphism of CYP2C19. Methods: A single oral dose of racemic lansoprazole (30 mg) was administered to 6 extensive metabolizers and 6 poor metabolizers whose genotypes were detd. by use of polymerase chain reaction-restriction fragment length polymorphism. The pharmacokinetic parameters were estd. from the blood plasma concns. of lansoprazole racemate, its enantiomers, and metabolites, which were measured for 24 h after drug administration. The unbound fraction of lansoprazole enantiomers was detd. by ultra-filtration of fresh human serum spiked with racemic lansoprazole. Results: The plasma concns. of R(+)-lansoprazole were consistently higher than those of the S(-)enantiomer in both extensive and poor metabolizers of CYP2C19, and the mean area under the plasma concn.-time curve of the (+)- and (-)-enantiomers showed 4.3- and 5.8-fold differences between poor and extensive metabolizers, resp. The (+)/(-) ratios of lansoprazole clearance were not significantly different between poor and extensive

metabolizers (0.19 and 0.05, resp.). The values for vol. of distribution of the (-)-enantiomer were 3- and 10-fold greater, resp., than those of the (+)-enantiomer in poor and extensive metabolizers, which was related to a 2-fold higher unbound fraction of the (-)-enantiomer. Conclusions: The effect of CYP2C19 genetic polymorphism on the enantioselective disposition of lansoprazole seems to be less significant than the effect on omeprazole and pantoprazole. The disposition of lansoprazole enantiomers appears to be influenced by enantioselective protein binding and by enantioselective metab. of lansoprazole.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT 103577-45-3, Lansoprazole 138530-94-6, (+)-Lansoprazole
138530-95-7, (-)-Lansoprazole
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enantioselective disposition of lansoprazole in extensive and poor metabolizers of CYP2C19)

L3 ANSWER 4 OF 28 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:428895 CAPLUS
DOCUMENT NUMBER: 137:11001
TITLE: Process for the crystallization of (R)- or (S)-lansoprazole
INVENTOR(S): Hashimoto, Hideo; Urai, Tadashi
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002044167	A1	20020606	WO 2001-JP10462	20011130
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002018506	A5	20020611	AU 2002-18506	20011130
JP 2002226478	A2	20020814	JP 2001-367473	20011130
EP 1337525	A1	20030827	EP 2001-998545	20011130
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
NO 2003002437	A	20030717	NO 2003-2437	20030528

PRIORITY APPLN. INFO.: JP 2000-367757 A 20001201
WO 2001-JP10462 W 20011130

AB The present invention relates to a prodn. method of a crystal of (R)-lansoprazole or (S)-lansoprazole, which includes crystn. at a temp. of 0.degree.-35.degree. from a C1-4 alkyl acetate soln. contg. (R)-lansoprazole or (S)-lansoprazole at a concn. of about 0.1 g/mL to about 0.5 g/mL and the like. According to the prodn. method of the present invention, a crystal of (R)-lansoprazole or (S)-lansoprazole superior in preservation stability can be produced efficiently on an industrial large scale.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT 138530-94-6P **138530-95-7P**, (S)-Lansoprazole
RL: IMF (Industrial manufacture); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method for crystn. of lansoprazole and oral prepns. contg. the same for treatment of digestive tract diseases)

L3 ANSWER 5 OF 28 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:881308 CAPLUS
DOCUMENT NUMBER: 137:163223
TITLE: Role of CYP3A4 and CYP2C19 in the stereoselective metabolism of lansoprazole by human liver microsomes
AUTHOR(S): Katsuki, H.; Hamada, A.; Nakamura, C.; Arimori, K.; Nakano, M.
CORPORATE SOURCE: Department of Pharmacy, Kumamoto University Hospital, Kumamoto, 860-8556, Japan
SOURCE: European Journal of Clinical Pharmacology (2001), 57(10), 709-715
CODEN: EJCPAS; ISSN: 0031-6970
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The aim of this investigation was to clarify the stereoselective properties in lansoprazole metab. by monitoring the metabolic consumption for each enantiomer and the formation of the main metabolites, lansoprazole sulfone and 5-hydroxylansoprazole, in the presence of human liver microsomal enzymes. Human liver microsomes or recombinant cytochrome P450 (CYP) enzymes were incubated with either (.+-.)-, (+)-, or (-)-lansoprazole in the presence of reduced NADP. The metabolic consumption of lansoprazole enantiomers was estd. from the amts. of enantiomers consumed by microsomal enzymes after incubation at 37.degree.C for 60 min. Metabolites of lansoprazole, lansoprazole sulfone, and 5-hydroxylansoprazole were detd. after incubation at 37.degree.C for 20 min, and kinetic parameters [Michaelis const. (Km) and max. velocity (Vmax)] were obtained using Eadie-Hofstee plots. (-)-Lansoprazole was metabolized more preferentially than (+)-lansoprazole in human liver microsomes. Stereoselective sulfoxidn. [(-)>(+)] and hydroxylation [(+)>(-)] were obsd. in human liver microsomes. Strikingly, in sulfoxidn., a significantly higher intrinsic clearance (Vmax,1/Km,1) of (-)-lansoprazole (0.023.+-.0.001 mL/min/mg) than (+)-lansoprazole (0.006.+-.0.000 mL/min/mg) was obsd. Consequently, sulfoxidn. is likely to play an important role in the stereoselective metab. of lansoprazole enantiomers. P450-isoform specificity for each enantiomer was evident. CYP3A4, which mainly catalyzed sulfoxidn., was more active toward (-)-lansoprazole in either a chiral or racemic drug as a substrate. CYP2C19, which catalyzed hydroxylation, preferentially metabolized (+)-lansoprazole. The consumption of (+)-lansoprazole was markedly inhibited by (-)-lansoprazole, indicating a metabolic enantiomer/enantiomer interaction. However, this alteration of recombinant CYP2C19 specificity for (+)-lansoprazole did not appear in metab. in human liver microsomes. Thus, stereoselective metab. was obsd. in human liver microsomes, and this stereoselectivity was mainly based on CYP3A4 specificity for preferable metab. of (-)-lansoprazole.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT 103577-45-3, (.+-.)-Lansoprazole 138530-94-6, (+)-Lansoprazole **138530-95-7**, (-)-Lansoprazole
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(role of CYP3A4 and CYP2C19 in the stereoselective metab. of

lansoprazole by human liver microsomes)

L3 ANSWER 6 OF 28 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:851149 CAPLUS
DOCUMENT NUMBER: 136:5990
TITLE: Process for producing crystal of optically active 2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methyl]sulfinyl]benzimidazole
INVENTOR(S): Hashimoto, Hideo; Maruyama, Hideaki
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001087874	A1	20011122	WO 2001-JP4014	20010515
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001056732	A5	20011126	AU 2001-56732	20010515
JP 2002037783	A2	20020206	JP 2001-144635	20010515
JP 3374314	B2	20030204		
JP 2002338567	A2	20021127	JP 2001-145688	20010515
JP 2003055372	A2	20030226	JP 2002-229402	20010515
EP 1293507	A1	20030319	EP 2001-930131	20010515
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003153766	A1	20030814	US 2002-275334	20021107

PRIORITY APPLN. INFO.: JP 2000-141670 A 20000515
JP 2001-144635 A3 20010515
WO 2001-JP4014 W 20010515

OTHER SOURCE(S): CASREACT 136:5990

AB Described is a process for producing crystals of (R)-2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methyl]-sulfinyl]benzimidazole [(R)-I].n'H2O (wherein n' is about 0 to about 0.1) or of a salt thereof, characterized by subjecting a soln. or dispersion in an org. solvent of (R)-2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methyl]sulfinyl]benzimidazole .nH2O (wherein n is about 0.1 to about 1.0) to crystn. to crystallize out the target compd. During examg. various methods of prepg. (R)- and (S)-I, it was found that there exist specific crystal forms for (R)- and (S)-I which are different from crystal forms of the sulfone deriv. When these isomers are crystd. in these specific crystal forms, surprisingly the sulfone deriv., which is normally difficult to remove, is readily removed to give the desired isomer with very high optical purity. Thereby, this process is a simple process by which an optically active sulfoxide deriv. can be efficiently and industrially mass-produced in high yield while attaining an extremely high enantiomer excess. (R)- and (S)-I possess antiulcer, anti-Helicobacter pylori, stomach-acid secretion inhibitory, and mucus membrane-protecting activity and are useful as antiulcer agents (no data). Thus, 0.747 L titanium isopropoxide was added to a mixt. of 4.5 kg 2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-

pyridyl]methyl]thio]benzimidazole (1.89% water content), 22 L PhMe, 25 g H2O, 0.958 L (+)-tartaric acid di-Et ester at 50-60.degree. and stirred at the same temp. for 30 min, followed by adding 0.733 L diisopropylethylamine at room temp. and then cumene hydroperoxide at -5.degree. to 5.degree., and the resulting mixt. was stirred at -5.degree. to 5.degree. for 1.5 h and treated with 17 L 30% sodium thiosulfate to decomp. the residual cumene hydroperoxide. The org. layer was sepd. and successively treated with H2O 4.5, heptane 13.5, tert-Bu Me ether 18, and heptane 27 L, and stirred at .apprx.10.degree. for crystn. The pptd. crystals were sepd. and washed with 4 L tert-Bu Me ether-PhMe (4:1) to give wet crystals of (R)-I contg. the sulfone deriv. by 0.90% and no sulfide and other isomer with optical purity of 100% ee. A suspension of the latter crystals in 20 L acetone was added dropwise to a mixt. of 7 L acetone and 34 L water and stirred at .apprx.10.degree. and the pptd. crystals were sepd. and washed with a mixt. of 4 L acetone and 12 L water to give wet crystals of (R)-I contg. no sulfone and sulfide deriv. and other isomer with optical purity of 100% ee. The latter wet crystals were dissolved in 45 L EtOAc and 3 L H2O and the org. layer was sepd., filtered to remove insol. matter, treated with 0.2 L Et3N, concd. to .apprx.7 L, and treated with 2.3L MeOH and then with .apprx.12.5% aq. NH3 (23 L, .apprx.50.degree.) and 22 L tert-Bu Me ether (.apprx.50.degree.). The org. layer was sepd. while saving the water layer and those in the following procedure, and treated with .apprx.12.5% aq. NH3, followed by sepg. the org. layer, and this procedure was repeated one more time. The sepd. water layers were combined, treated with 22 L EtOAc, adjusted to pH .apprx.8 by adding dropwise AcOH, followed by sepg. the org. layer and extg. the water layer with 11 L EtOAc. The org. layers were combined, washed with 11 L .apprx.20% aq. NaCl, treated with 0.2 L Et3N, concd. under reduced pressure, treated with 5 L acetone, and concd. under reduced pressure. The conc. was dissolved in 9 L acetone and the soln. was added dropwise to a mixt, of 4.5 L acetone and 22.5 L H2O, followed by adding dropwsie 18 L water to the resulting mixt. The resulting mixt. was stirred at .apprx.10.degree. and the pptd. crystals were sepd. and successively washed with a cold 1:3 mixt. of acetone and water (3 L) and then 12 L water to give wet crystals of (R)-I contg. no sulfone and sulfide deriv. and other isomer with optical purity of 100% ee. The latter wet crystals were dissolved in 32 L EtOAc, followed by sepg. the water layer, and the org. layer was concd. under reduced pressure to .apprx.14 L, treated with 36 L EtOAc and 270 g activated charcoal, stirred, and filtered to remove the activated charcoal. The filtrate was concd. under reduced pressure to .apprx.14 L, followed by adding 90 L heptane to the conc. at .apprx.40.degree. and stirring the resulting mixt. at .apprx.40.degree. for 30 min., and the pptd. crystals were sepd., washed with a 1:8 mixt. of EtOAc and heptane (6 L), and dried to give 3.4 kg (R)-I contg. no sulfone and sulfide deriv. and other isomer with optical purity of 100% ee, which had specific peaks in powder X-ray diffraction anal.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT 138530-94-6P **138530-95-7P**
RL: IMF (Industrial manufacture); PEP (Physical, engineering or chemical process); PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(process for producing optically active [[[methyl(fluoroethoxy)pyridyl] methyl]sulfinyl]benzimidazole in specific crystal forms by crystn.)

L3 ANSWER 7 OF 28 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:816657 CAPLUS
DOCUMENT NUMBER: 135:357923
TITLE: Process for producing optically active

pyridylmethylsulfinylbenzimidazole derivatives

INVENTOR(S): Hashimoto, Hideo; Urai, Tadashi
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., USA

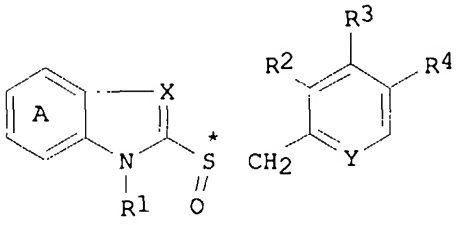
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001083473	A1	20011108	WO 2001-JP3613	20010426
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001052595	A5	20011112	AU 2001-52595	20010426
EP 1277752	A1	20030122	EP 2001-925946	20010426
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2002012592	A2	20020115	JP 2001-130660	20010427
US 2003171591	A1	20030911	US 2002-276109	20021024

PRIORITY APPLN. INFO.: JP 2000-128760 A 20000428
WO 2001-JP3613 W 20010426

OTHER SOURCE(S): CASREACT 135:357923; MARPAT 135:357923

GI



I

AB This document discloses a process for producing an optically active isomer of a compd. represented by the formula I (wherein ring A represents an optionally substituted benzene ring; R1 represents hydrogen, an optionally substituted hydrocarbon group, acyl, or acyloxy; R2, R3, and R4 each represents hydrogen, optionally substituted alkyl, optionally substituted alkoxy, or optionally substituted amino; X represents nitrogen or CH; Y represents nitrogen or CH; and the asterisk indicates an asym. center) characterized by reacting a pyridylmethylthiobenzimidazole deriv. with an excess of an oxidizing agent in the presence of a catalyst for asymmetry induction. Compds. I are antiulcer agents (no data). This process is a simple process by which an optically active sulfoxide deriv. can be efficiently and industrially mass-produced in high yield while attaining an extremely high enantiomer excess.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT 73590-58-6P 103577-45-3P 138530-94-6P **138530-95-7P**

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process for producing optically active pyridylmethylsulfinylbenzimidazole derivs.)

L3 ANSWER 8 OF 28 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:314800 CAPLUS
DOCUMENT NUMBER: 135:116434
TITLE: High-performance liquid chromatographic assay for the simultaneous determination of lansoprazole enantiomers and metabolites in human liver microsomes
AUTHOR(S): Katsuki, H.; Hamada, A.; Nakamura, C.; Arimori, K.; Nakano, M.
CORPORATE SOURCE: Department of Pharmacy, Kumamoto University Hospital, Kumamoto, 860-8556, Japan
SOURCE: Journal of Chromatography, B: Biomedical Sciences and Applications (2001), 757(1), 127-133
CODEN: JCBBEP; ISSN: 0378-4347
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A simple, sensitive and enantioselective HPLC method was developed for the simultaneous detn. of lansoprazole enantiomers: a proton pump inhibitor, and its major metabolites: 5-hydroxylansoprazole and lansoprazole sulfone in human liver microsomes. After extn. from the microsomal incubation mixt. with a Et2O-CH2Cl2 (7:3, vol./vol.) mixt., analytes were measured by reversed-phase HPLC on a Chiralcel.RTM. OD-R column. Detection was made using an UV absorbance detector set at a wavelength of 285 nm. The mobile phase consisted of a MeOH-H2O (75:25, vol./vol.) mixt. At a flow-rate of 0.5 mL/min, the total run time was 35 min. The limit of quantification for both lansoprazole enantiomers was 0.25 .mu.M and for the metabolites 0.13 .mu.M The method is suitable for the anal. of lansoprazole enantiomers and its metabolites from human microsomal liver incubations.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
IT 131926-98-2, 5-Hydroxylansoprazole 131926-99-3, Lansoprazole sulfone 138530-94-6, (+)-Lansoprazole **138530-95-7**, (-)-Lansoprazole
RL: ANT (Analyte); ANST (Analytical study)
(high-performance liq. chromatog. assay for the simultaneous detn. of lansoprazole enantiomers and metabolites in human liver microsomes)

L3 ANSWER 9 OF 28 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:167501 CAPLUS
DOCUMENT NUMBER: 134:347944
TITLE: Pharmacokinetic differences between lansoprazole enantiomers and contribution of cytochrome P450 isoforms to enantioselective metabolism of lansoprazole in dogs
AUTHOR(S): Masa, Kengo; Hamada, Akinobu; Arimori, Kazuhiko; Fujii, Junko; Nakano, Masahiro
CORPORATE SOURCE: Department of Pharmacy, Kumamoto University Hospital, Kumamoto, 860-8556, Japan
SOURCE: Biological & Pharmaceutical Bulletin (2001), 24(3), 274-277
CODEN: BPBLEO; ISSN: 0918-6158
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The purpose of this study was to evaluate the pharmacokinetics of lansoprazole enantiomers and contribution of cytochrome P 450 enzymes to

enantioselective metab. in dogs. The mean Cmax and area under the curve (AUC) values of (+)-lansoprazole were 4-5 times greater than those of (-)-lansoprazole following oral administration of 30-mg racemic lansoprazole to dogs. The CLtot/F values of (+)-lansoprazole were significantly smaller than those of (-)-lansoprazole ($p<0.05$). The mean unbound fraction of (-)-lansoprazole was significantly greater than that of the (+)-lansoprazole. The amt. of (+)-lansoprazole remaining was significantly greater than that of the (-)-lansoprazole after incubation of racemic lansoprazole in dog liver microsomes. When the effects of ticlopidine or ketoconazole on the metab. of lansoprazole were studied using dog liver microsomes, ticlopidine significantly inhibited the formation of 5-hydroxylansoprazole, but not another metabolite, lansoprazole sulfone; however ketoconazole significantly inhibited formation of both metabolites. When the amt. of (+)- and (-)-enantiomers remaining was measured in the presence and absence of ticlopidine, the amt. of (+)-lansoprazole was significantly greater than that of the (-)-lansoprazole. On the other hand, there was no significant difference between the amt. of (+)- and (-)-enantiomers remaining in combination with ketoconazole. These results suggest that the enantioselective pharmacokinetics of lansoprazole enantiomers are probably ascribable to their enantioselective protein binding and/or metab., and among the cytochrome P 450 enzymes, CYP3A contributed to the enantioselective metab. of lansoprazole.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

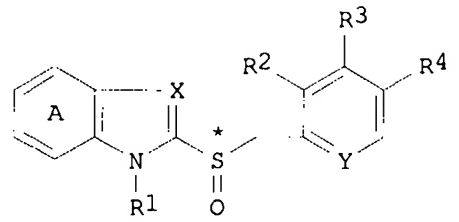
IT 131926-98-2, 5-Hydroxylansoprazole 131926-99-3, Lansoprazole sulfone 138530-94-6, (+)-Lansoprazole **138530-95-7**, (-)-Lansoprazole
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); PRP (Properties); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(pharmacokinetic differences between lansoprazole enantiomers and contribution of cytochrome P 450 isoforms to enantioselective metab. of lansoprazole in dogs)

L3 ANSWER 10 OF 28 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:152672 CAPLUS
DOCUMENT NUMBER: 134:193436
TITLE: Process for preparation of optically active sulfoxide derivatives by asymmetric oxidation of sulfide
INVENTOR(S): Kawada, Mitsuru; Yamano, Toru; Taya, Naohiro
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

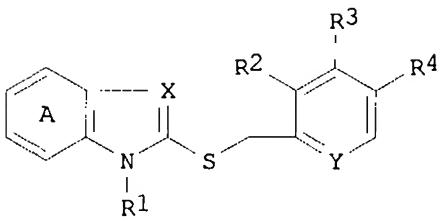
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001014366	A1	20010301	WO 2000-JP5682	20000824
W: AE, AG, AL, AM, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
JP 2001131172	A2	20010515	JP 2000-253771	20000824

PRIORITY APPLN. INFO.: JP 1999-238471 A 19990825

OTHER SOURCE(S): CASREACT 134:193436; MARPAT 134:193436
GI



I



II

AB Optically active compds. represented by general formula (I; wherein ring A is an optionally substituted benzene ring; R1 is H, optionally substituted aralkyl, acyl, or acyloxy; R2, R3 and R4 are each H, optionally substituted alkyl, optionally substituted alkoxy, or optionally substituted NH2; X and Y are N or CH; and * represents an asym. center) or salts thereof are prepd. easily and in an extremely high enantiomeric excess and a high yield by oxidizing compds. represented by general formula (II; ring A, R1-R4 , X, and Y are defined as above) or salts thereof in the presence of both a substance acting as a mol. sieve and an asym. induction catalyst. This process efficiently gives in a large industrial scale, I which possess antiulcer activity (no data). Thus, 2.1 g 2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methyl]thio]-1H-benzimidazole contg. 105 .mu.L H2O and 2.1 g mol. sieve 4A were mixed, followed by adding 120 .mu.L H2O to make a total water content of 12.5 mmol, and 50 mL PhMe in this order, and the resulting mixt. was stirred for 15 min, treated with 2.6 mL (-)-tartaric acid di-Et ester and 1.8 mL titanium(IV) isopropoxide in this order, stirred at 50.degree. for 1 h, and then treated with 1.0 mL i-Pr2NEt and 0.9 mL cumene hydroperoxide in this order and stirred for 3 h to give 77% (S)-2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methyl]sulfinyl]-1H-benzimidazole (95% ee).

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT 138530-94-6P **138530-95-7P** 326927-11-1P 326927-12-2P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of optically active [(pyridylmethyl)sulfinyl]benzimidazole derivs. as antiulcer agents by asym. oxidn. of [(pyridylmethyl)thio]benzimidazole derivs.)

L3 ANSWER 11 OF 28 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:31493 CAPLUS
DOCUMENT NUMBER: 134:86261
TITLE: Crystals of benzimidazole compounds
INVENTOR(S): Fujishima, Akira; Aoki, Isao; Kamiyama, Keiji
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 22 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001002389	A1	20010111	WO 2000-JP4279	20000629
W: AE, AG, AL, AM, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
JP 2001072675	A2	20010321	JP 2000-195627	20000629
EP 1191025	A1	20020327	EP 2000-942388	20000629
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6608092	B1	20030819	US 2001-19254	20011228

PRIORITY APPLN. INFO.: JP 1999-186403 A 19990630
WO 2000-JP4279 W 20000629

AB Cryst. S-isomer of 2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridinyl]methyl]sulfinyl]-1H-benzimidazole (I) or salts thereof, useful as antiulcer agents at 5-150 mg/day p.o., are prepd. and their crystal structures detd. by powder x-ray diffraction. Chromatog. resoln. of racemic I on a Chiralcel OD column with 85:15 hexane/isopropanol mobile phase gave amorphous (S)-I of 93.3% ee, which was dissolved in acetone, the soln. was gently heated while adding H2O, the soln. was kept at room temp. overnight and subject to repeated supersonic treatment and recrystn. to give cryst. (S)-I of 99.4% ee.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT **138530-95-7P** 318290-63-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(crystals of benzimidazole compds.)

L3 ANSWER 12 OF 28 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:555845 CAPLUS
DOCUMENT NUMBER: 133:305113
TITLE: A QSERR study on enantioselective separation of enantiomeric sulphoxides
AUTHOR(S): Montanari, C. A.; Cass, Q. B.; Tiritan, M. E.; Souza, A. L. S. d.
CORPORATE SOURCE: Nucleo de Estudos em Quimica Medicinal -NEQUIM, Departamento de Quimica, Universidade Federal de Minas Gerais, Belo Horizonte, 31270-901, Brazil
SOURCE: Analytica Chimica Acta (2000), 419(1), 93-100
CODEN: ACACAM; ISSN: 0003-2670
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A set of chiral sulfoxides was chromatographed on four chiral stationary phases (CSPs), using cellulose and amylose tris-phenylcarbamates coated onto 3-aminopropyl mesoporous silica. The relative retention and enantioselectivities of the solutes were compared to mol. connectivity indexes, similarity and holistic descriptors calcd. by 3D-WHIM. Many

quant. structure-enantioselective retention relations were developed to describe the enantioselective chromatog. performance. The same dataset was used for all CSPs, and it was possible to reveal a clear distinction between them, i.e. there was a mol. recognition pattern established according to CSPs. Also log k could be predicted for both sulfoxide enantiomers, but .alpha. was not discriminated.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT 824-86-2 833-82-9 934-72-5 1193-82-4 1517-78-8 1519-39-7
2169-00-8 2843-91-6 4850-71-9 5056-07-5 7417-77-8 7417-81-4
10381-68-7 14090-81-4 14090-83-6 16487-10-8 18453-46-8
20246-02-0 20451-53-0 42872-16-2 60349-76-0 60349-79-3
63865-78-1 63865-79-2 79888-64-5 79888-65-6 89004-04-6
89299-85-4 89299-86-5 93974-18-6 95126-91-3 102340-68-1
103577-45-3 132747-03-6 138530-94-6 **138530-95-7**
142235-66-3 142235-67-4 153782-37-7 159280-43-0 159280-47-4
160998-20-9 160998-21-0 160998-22-1 160998-24-3 161104-29-6
161104-30-9 161104-33-2 161104-34-3 161104-35-4 161104-36-5
161104-37-6 161249-13-4 169332-19-8
RL: ANT (Analyte); PEP (Physical, engineering or chemical process); ANST (Analytical study); PROC (Process)
(QSERR study on enantioselective sepn. of enantiomeric sulfoxides)

L3 ANSWER 13 OF 28 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:416841 CAPLUS
DOCUMENT NUMBER: 133:17460
TITLE: Inclusion and resolution process in preparation of optical pure benzimidazoles as medicines useful in resisting peptic ulcers
INVENTOR(S): Deng, Jingen; Chi, Yongxiang; Zhu, Jin; Peng, Xiaohua; Jiang, Yaozhong; Fu, Fangmin; Cui, Xin
PATENT ASSIGNEE(S): Chengdu Inst. of Organic Chemistry, Chinese Academy of Sciences, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 12 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1223262	A	19990721	CN 1998-124029	19981228
CN 1087739	B	20020717		

PRIORITY APPLN. INFO.: CN 1998-124029 19981228

AB Six benzimidazole-type antiulcer agents timoprazole, picoprazole, omeprazole, lansoprazole, pantoprazole, and E-3,810 are resolved by embedding antiulcer agent with optical purity embedding agent at a mole ratio of 1:0.5-2.0 in org. solvent at 60-130.degree. for 12-72 h, standing at (-20)-10.degree. for 6-36 h, filtering to obtain one optical configuration solid inclusion compd. and another optical configuration filtrate, sepg. resp. solid and filtrate by silica gel column with EtOAc-petroleum ether (1:1-5)-alc. as gradient eluent, and/or recrystg. in haloalkane-ether (1:05-6) to obtain racemic solid and optical purity filtrate. The embedding agent is selected from 6,6'-di(R1)-2,2'-dihydroxy-1,1'-binaphthyl, 10,10'-dihydroxy-9,9'-biphenanthrenyl, trans-2-R2-4,5-di(.alpha.-hydroxy-.alpha.-phenylbenzyl)-1,3-dioxolane, and R3-CO-CH(O-R4)-CH(O-R4)-CO-R3 (R1 = H, Br, or CH3; R2 = H, cyclohexyl, or cyclopentyl; R3 = H, Et, NMe2, or N(C6H11)2; and R4 = H, or CH3); the org. solvent from arene, acetonitrile, and arene-n-hexane (0.5-6:1); and the alc. from one or more of ethanol, methanol, isopropanol, and butanol.

IT 119141-88-7P 119141-89-8P **138530-95-7P** 177795-59-4P
RL: PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(inclusion and resoln. process in prepn. of optical pure benzimidazoles as medicines useful in resisting peptic ulcers)

L3 ANSWER 14 OF 28 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:302012 CAPLUS
DOCUMENT NUMBER: 132:307370
TITLE: Manufacture of pyridines with fungi
INVENTOR(S): Nagasawa, Toru; Tsujii, Masahiko
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2000125895	A2	20000509	JP 1999-233440	19990820

PRIORITY APPLN. INFO.: JP 1998-234007 19980820
OTHER SOURCE(S): MARPAT 132:307370
AB Compds. (e.g. sulfoxides) are manufd. by cultivation of fungi in the presence of starting materials (e.g. thio ethers). Cunninghamella echinulata was shake-cultured in a medium contg. 2-[4-(3-methoxypropoxy)-3-methylpyridin-2-yl]methylthiobenzimidazole to manuf. (S)-rabeprazole.
IT 119141-88-7P **138530-95-7P** 177795-59-4P
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(manuf. of sulfoxides from thio ethers with fungi)

L3 ANSWER 15 OF 28 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:795602 CAPLUS
DOCUMENT NUMBER: 132:35699
TITLE: Multibinding inhibitors of H+K+-ATPase
INVENTOR(S): Meier-davis, Susan; Griffin, John H.; Choi, Seok-Ki
PATENT ASSIGNEE(S): Advanced Medicine, Inc., USA
SOURCE: PCT Int. Appl., 182 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 27
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9963940	A2	19991216	WO 1999-US12925	19990608
WO 9963940	A3	20010607		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6288234	B1	20010911	US 1999-325662	19990604
CA 2319477	AA	19991216	CA 1999-2319477	19990608

SG 80631	A1	20010522	SG 1999-2719	19990608
EP 1143991	A2	20011017	EP 1999-930182	19990608
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
SG 90053	A1	20020723	SG 1999-2944	19990608
US 6566509	B1	20030520	US 1999-327899	19990608
ZA 2000004086	A	20010810	ZA 2000-4086	20000810
ZA 2000004558	A	20011130	ZA 2000-4558	20000831
ZA 2000004559	A	20020402	ZA 2000-4559	20000831
US 2002028943	A1	20020307	US 2001-760827	20010117
US 2003176670	A1	20030918	US 2002-330381	20021227

PRIORITY APPLN. INFO.:

US 1998-88448P	P	19980608
US 1998-93072P	P	19980716
US 1999-325662	A3	19990604
US 1999-327899	A1	19990608
WO 1999-US12925	W	19990608

AB Disclosed are multibinding compds., LpXq [where L = a ligand which is an inhibitor of H+/K+-ATPase; X = a linker; p = 2-10; q = 1-20], which inhibit H+/K+-ATPase, an enzyme which is involved in the control of acid secretion in the stomach. Combinatorial arrays, methods of synthesis, and methods of assaying the dimeric and multimeric compds. are also embodied by the invention. A no. of divalent prophetic examples, derived from substituted benzimidazoles and difunctional linkers, are given. The multibinding compds. of this invention are useful in the treatment gastroesophageal reflux disease (GERD) and peptic ulcer disease (no data). The multibinding compds. provide greater biol. and/or therapeutic effects than the aggregate of the unlinked ligands due to their multibinding properties (no data). H+/K+-ATPase inhibitor ligands include omeprazole, (S)-omeprazole, pantoprazole, (S)-pantoprazole, lansoprazole, (S)-lansoprazole, rabeprazole,leminoprazole, IY-81149, RO-18-5364, AD-8240, Sch 28080, H-33525, SK&F-97574,SK&F-96067, and YH1885.

IT 73590-58-6DP, Omeprazole, dimeric and multimeric derivs. of 76081-98-6DP, Sch 28080, dimeric and multimeric derivs. of 101387-98-8DP, RO-18-5364, dimeric and multimeric derivs. of 102625-70-7DP, Pantoprazole, dimeric and multimeric derivs. of 103577-45-3DP, Lansoprazole, dimeric and multimeric derivs. of 104340-86-5DP, Leminoprazole, dimeric and multimeric derivs. of 115607-61-9DP, SK&F-96067, dimeric and multimeric derivs. of 117976-89-3DP, Rabeprazole, dimeric and multimeric derivs. of 119141-88-7DP, (S)-Omeprazole, dimeric and multimeric derivs. of **138530-95-7DP**, (S)-Lansoprazole, dimeric and multimeric derivs. of 144453-77-0DP, SK&F-97574, dimeric and multimeric derivs. of 172152-36-2DP, IY-81149, dimeric and multimeric derivs. of 178307-42-1DP, YH1885, dimeric and multimeric derivs. of 252551-67-0DP, (S)-Pantoprazole, dimeric and multimeric derivs. of
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compd.; prepn. of multibinding inhibitors of H+K+-ATPase for the treatment of gastroesophageal reflux disease and peptic ulcer disease)

L3 ANSWER 16 OF 28 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER:	1999:495175 CAPLUS
DOCUMENT NUMBER:	131:134655
TITLE:	S-lansoprazole compositions and methods
INVENTOR(S):	Barberich, Timothy J.; Yelle, William E.; Rubin, Paul D.
PATENT ASSIGNEE(S):	Sepracor Inc., USA
SOURCE:	PCT Int. Appl., 23 pp.
	CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9938512	A1	19990805	WO 1999-US1920	19990129
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2320902	AA	19990805	CA 1999-2320902	19990129
AU 9924818	A1	19990816	AU 1999-24818	19990129
EP 1056457	A1	20001206	EP 1999-904418	19990129
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002501896	T2	20020122	JP 2000-529245	19990129
US 2001025107	A1	20010927	US 2001-854065	20010511

PRIORITY APPLN. INFO.:
US 1998-73141P P 19980130
US 1998-107460P P 19981105
US 1999-240262 A1 19990129
WO 1999-US1920 W 19990129

AB Methods and compns. are disclosed utilizing optically pure (-)-lansoprazole for the treatment of ulcers in humans while substantially reducing the concomitant liability of adverse effects assocd. with the racemic mixt. of lansoprazole. The optically pure (-) isomer is also useful for the treatment of gastroesophageal reflux. (-)-Lansoprazole is an inhibitor of H+ release and is therefore useful in the treatment of other conditions related to gastric hypersecretion such as Zollinger-Ellison Syndrome.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT **138530-95-7**, (-)-Lansoprazole
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral compns. contg. optically pure S-lansoprazole)

L3 ANSWER 17 OF 28 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:1517 CAPLUS
DOCUMENT NUMBER: 130:177083
TITLE: Pharmacokinetic differences between lansoprazole enantiomers in rats
AUTHOR(S): Arimori, Kazuhiko; Yasuda, Kazuto; Katsuki, Hisakazu; Nakano, Masahiro
CORPORATE SOURCE: Department of Pharmacy, Kumamoto University Hospital, Kumamoto, 860-8556, Japan
SOURCE: Journal of Pharmacy and Pharmacology (1998), 50(11), 1241-1245
CODEN: JPPMAB; ISSN: 0022-3573
PUBLISHER: Royal Pharmaceutical Society of Great Britain
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Because limited information is available about potential differences between the pharmacokinetics and pharmacodynamics of the enantiomers of lansoprazole, the enantioselective pharmacokinetics of the compd. have

been investigated in rats. There was a noticeable difference between the serum levels of the enantiomers of lansoprazole and of their metabolites, 5-hydroxylansoprazole enantiomers, after oral administration of the racemate (50 mg kg-1) to rats. Cmax (max. serum concn.) and AUC (area under the serum concn.-time curve) for (+)-lansoprazole were 5-6 times greater than those for (-)-lansoprazole, whereas for (+)-5-hydroxylansoprazole both values were significantly smaller than those for the (-) enantiomer. CLtot/F values (where CLtot is total clearance and F is the fraction of the dose absorbed) for (+)-lansoprazole were significantly smaller than those for the (-) enantiomer. There was no significant difference between the absorption rate consts. of the lansoprazole enantiomers in the in-situ absorption study. The in-vitro protein-binding study showed that binding of (+)-lansoprazole to rat serum proteins was significantly greater than for the (-) enantiomer. The in-vitro metabolic study showed that the mean metabolic ratio (45.cntdot.9%) for (-)-lansoprazole was significantly greater than that (19.cntdot.8%) for the (+) enantiomer in rat liver microsomes at 5.cntdot.6 .mu.M lansoprazole. These results show that the enantioselective disposition of lansoprazole could be a consequence of the enantioselectivity of plasma-protein binding and the hepatic metab. of the enantiomers.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT 138530-94-6, (+)-Lansoprazole **138530-95-7**, (-)-Lansoprazole 220609-28-9 220609-30-3
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pharmacokinetic differences between lansoprazole enantiomers in rats)

L3 ANSWER 18 OF 28 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:169634 CAPLUS
DOCUMENT NUMBER: 128:175755
TITLE: Separation of lansoprazole enantiomers in human serum by HPLC
AUTHOR(S): Borner, K.; Borner, E.; Lode, H.
CORPORATE SOURCE: Inst. Klinische Chem. Pathobiochem., Klin. Benjamin Franklin, Berlin, D-12200, Germany
SOURCE: Chromatographia (1998), 47(3/4), 171-175
CODEN: CHRGB7; ISSN: 0009-5893
PUBLISHER: Friedrich Vieweg & Sohn Verlagsgesellschaft mbH
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A new and simple HPLC is described for the sepn. and quant. detn. of the (+)and (-)-enantiomers of lansoprazole. The analytes were extd. from blood serum as previously described for whole lansoprazole. The enantiomers were sepd. by chromatog. on a CHIRAL-AGPR column which contained covalently bound acid .alpha.1-glycoprotein as chiral selector. In the pure drug the (-)/(+) ratio was 0.99:1.01. In serum the concn. of the (-)-enantiomer was 3-5 times higher than that of the (+)-enantiomer. Both enantiomers differ remarkably in their pharmacokinetics.

IT 103577-45-3, Lansoprazole 138530-94-6, (+)-Lansoprazole **138530-95-7**, (-)-Lansoprazole
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(lansoprazole enantiomers in blood serum sepd. by HPLC)

L3 ANSWER 19 OF 28 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:204119 CAPLUS
DOCUMENT NUMBER: 126:186087
TITLE: Optical purification of enantiomerically enriched 2-[(arylmethyl)sulfinyl]benzimidazole derivatives

INVENTOR(S): Von Unge, Sverker
PATENT ASSIGNEE(S): Astra Aktiebolag, Swed.; Von Unge, Sverker
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9702261	A1	19970123	WO 1996-SE841	19960626
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
ZA 9605205	A	19970103	ZA 1996-5205	19960619
TW 444010	B	20010701	TW 1996-85107517	19960622
CA 2226184	AA	19970123	CA 1996-2226184	19960626
AU 9663240	A1	19970205	AU 1996-63240	19960626
AU 698638	B2	19981105		
EP 836601	A1	19980422	EP 1996-922339	19960626
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
CN 1193971	A	19980923	CN 1996-196465	19960626
CN 1098261	B	20030108		
BR 9609450	A	19990302	BR 1996-9450	19960626
JP 11508590	T2	19990727	JP 1996-505063	19960626
RU 2144031	C1	20000110	RU 1998-101727	19960626
IL 122811	A1	20001121	IL 1996-122811	19960626
EE 3444	B1	20010615	EE 1997-368	19960626
US 5929244	A	19990727	US 1996-676215	19960719
NO 9706030	A	19980209	NO 1997-6030	19971222

PRIORITY APPLN. INFO.: US 1995-491939 A2 19950703
WO 1995-SE817 A 19950703
WO 1996-SE841 W 19960626

AB The title process for purifn. of, e.g., omeprazole comprises crystn. of the racemate from a soln. of an enantiomerically or diastereomerically enriched prepn. followed by recovery of the purified. compd.

IT 119141-88-7P, (-)-Omeprazole 138530-94-6P, (+)-Lansoprazole **138530-95-7P**, (-)-Lansoprazole 177541-00-3P, Benzenamine, 2-[(1H-benzimidazol-2-ylsulfinyl)methyl]-N-methyl-N-(2-methylpropyl)-, (-)- 177541-01-4P, Benzenamine, 2-[(1H-benzimidazol-2-ylsulfinyl)methyl]-N-methyl-N-(2-methylpropyl)-, (+)- 177795-59-4P 177795-60-7P 187589-30-6P
RL: IMF (Industrial manufacture); PUR (Purification or recovery); PREP (Preparation)
(optical purifn. of enantiomerically enriched 2-[(arylmethyl)sulfinyl]benzimidazole derivs.)

L3 ANSWER 20 OF 28 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:76137 CAPLUS
DOCUMENT NUMBER: 126:176973
TITLE: Chiral resolution of pantoprazole sodium and related sulfoxides by complex formation with bovine serum albumin in capillary electrophoresis
AUTHOR(S): Eberle, Daniela; Hummel, Rolf Peter; Kuhn, Reinhard
CORPORATE SOURCE: Research Laboratories Byk Gulden, Konstanz, Germany
SOURCE: Journal of Chromatography, A (1997), 759(1 + 2),

185-192
CODEN: JCRAEY; ISSN: 0021-9673
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The sepn. of enantiomers of pantoprazole sodium, omeprazole and lansoprazole by capillary zone electrophoresis using bovine serum albumin (BSA) as the chiral selector is described. Baseline sepn. of the three structurally related drugs was obtained after optimization of the most important exptl. parameters. For this purpose, influences such as BSA concn., pH and concn. of 1-propanol as org. modifier on the sepn. were investigated. Increasing concns. of BSA improved the chiral resoln. but lowered the sensitivity of the detection system. Discrimination of the enantiomers was obsd. only in a narrow pH range of 7-8. An optimum of pH 7.4 was a good compromise in terms of enantio-resoln. and peak shape. 1-Propanol when added to the buffer system, improved the peak shape of the analytes and the resoln. The optimized method has been validated for pantoprazole sodium and is useful for routine anal.

IT 73590-58-6, Omeprazole 102625-70-7, Pantoprazole 103577-45-3, Lansoprazole 119141-88-7 119141-89-8 138530-94-6 **138530-95-7** 142678-35-1 142706-18-1
RL: ANT (Analyte); ANST (Analytical study)
(resoln. of pantoprazole, omeprazole and lansoprazole by capillary electrophoresis)

L3 ANSWER 21 OF 28 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:353180 CAPLUS
DOCUMENT NUMBER: 125:58516
TITLE: Preparation of unsymmetrical heterocyclylsulfoxide enantiomers
INVENTOR(S): Larsson, Erik Magnus; Stenhede, Urban Jan; Soerensen, Henrik; Von Unge, Per Oskar Sverker; Cotton, Hanna Kristina
PATENT ASSIGNEE(S): Astra Aktiebolag, Swed.
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9602535	A1	19960201	WO 1995-SE818	19950703
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
SE 9402510	A	19960116	SE 1994-2510	19940715
SE 504459	C2	19970217		
RU 2157806	C2	20001020	RU 1997-102162	19950703
EE 3354	B1	20010215	EE 1997-6	19950703
AT 242233	E	20030615	AT 1995-926068	19950703
CA 2193994	AA	19960201	CA 1995-2193994	19950705
AU 9529948	A1	19960216	AU 1995-29948	19950705
AU 688074	B2	19980305		
EP 773940	A1	19970521	EP 1995-926068	19950705
EP 773940	B1	20030604		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

CN 1157614	A	19970820	CN 1995-194956		19950705
CN 1070489	B	20010905			
HU 76642	A2	19971028	HU 1997-108		19950705
BR 9508292	A	19971223	BR 1995-8292		19950705
JP 10504290	T2	19980428	JP 1995-504938		19950705
IL 114477	A1	20010724	IL 1995-114477		19950706
ZA 9505724	A	19960115	ZA 1995-5724		19950710
US 5948789	A	19990907	US 1995-492087		19950714
FI 9700102	A	19970110	FI 1997-102		19970110
NO 9700153	A	19970114	NO 1997-153		19970114
PRIORITY APPLN. INFO.:			SE 1994-2510	A	19940715
			WO 1995-SE818	W	19950703

OTHER SOURCE(S): CASREACT 125:58516; MARPAT 125:58516

AB Enantiomeric R1ZSOR2 [R1 = (un)substituted 2-pyridyl, (un)substituted 2-(R4R5N)C6H4; R2 = (un)substituted 2-benzimidazolyl, thieno[3,4-d]imidazol-2-yl, etc.; R4,R5 = H, (ar)alkyl; Z = CH2, (un)substituted 1,2-phenylene, etc.] were prepd. by oxidn. of prochiral R1ZSR2 in the presence of a chiral Ti complex and a base.

IT 138530-94-6P **138530-95-7P** 142678-35-1P 142706-18-1P
154461-48-0P 156601-78-4P 156601-79-5P 170431-13-7P 170431-14-8P
175078-93-0P 177540-97-5P 177540-98-6P 177540-99-7P 177541-00-3P
177541-01-4P 177541-02-5P 177541-03-6P 177795-59-4P 177795-60-7P
177932-96-6P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of unsym. heterocyclylsulfoxide enantiomers)

L3 ANSWER 22 OF 28 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1996:229899 CAPLUS
DOCUMENT NUMBER: 124:331460
TITLE: Determination of R(+)- and S(-)-lansoprazole using chiral stationary-phase liquid chromatography and their enantioselective pharmacokinetics in humans
AUTHOR(S): Katsuki, Hisakazu; Yagi, Hatsumi; Arimori, Kazuhiko; Nakamura, Chizuko; Nakano, Masahiro; Katafuchi, Shigeru; Fujioka, Yuhichi; Fujiyama, Shigetoshi
CORPORATE SOURCE: Dep. Pharmacy, Kumamoto Univ. Hospital, Kumamoto, Japan
SOURCE: Pharmaceutical Research (1996), 13(4), 611-15
CODEN: PHREEB; ISSN: 0724-8741
PUBLISHER: Plenum
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Stereoselective and sensitive methods employing chiral stationary phase columns for HPLC detn. of enantiomers of lansoprazole in the human serum were developed and pharmacokinetic behaviors of the enantiomers were evaluated in seven subjects. Five chiral stationary phase columns: Chiralcel OD (cellulose tris(3,5-dimethyl-phenylcarbamate)), OF (cellulose tris(4-chlorophenylcarbamate)), OG (cellulose tris(4-methylphenylcarbamate)) and OJ (cellulose tris(4-methylbenzoate)), and Chiralpak AS (amylose tris ((S)-1-phenylethylcarbamate)) were investigated. Chiralcel OD and Chiralpak AS columns gave a good resoln. of R(+)- and S(-)-enantiomers from racemic lansoprazole, but Chiralcel OF, OG, and OJ did not. The mean Cmax and the AUC values of R(+)-enantiomer were 3-5 times greater than those of S(-)-enantiomer following oral administration of 30 mg of racemic lansoprazole. The CLtot values of R(+)-enantiomer were significantly smaller than those of S(-)-enantiomer. Binding of R(+)-enantiomer to human serum proteins was significantly greater than that of S(-)-enantiomer. The mean metabolic ratio (metabolites/parent compd.) in human liver microsomes of S(-)-enantiomer

was significantly greater than that of R(+)-enantiomer. The stereoselective pharmacokinetics of lansoprazole enantiomers is likely due to its stereoselective protein binding and/or metab.

IT 138530-94-6, R(+)-Lansoprazole **138530-95-7**, (-)-Lansoprazole
RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(detn. of R(+)- and S(-)-lansoprazole using chiral stationary-phase liq. chromatog. and their enantioselective pharmacokinetics in humans)

L3 ANSWER 23 OF 28 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:148866 CAPLUS
DOCUMENT NUMBER: 124:305977
TITLE: Enantiomeric resolution of chiral sulfoxides on polysaccharide phases by HPLC
AUTHOR(S): Matlin, Stephen A.; Tiritan, M. Elizabeth; Cass, Quezia B.; Boyd, Derek R.
CORPORATE SOURCE: Dep. Chem., University Warwick, Coventry, UK
SOURCE: Chirality (1996), 8(1), 147-52
CODEN: CHRLEP; ISSN: 0899-0042
PUBLISHER: Wiley-Liss
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The enantiomeric resoln. of chiral sulfoxides was studied on amylose (S)-.alpha.-methylbenzyl carbamate phase coated on aminopropylated 7 .mu.m silica with 500 .ANG. diam. pores. This is very successful in the sepn. of alkyl/aryl, aryl/aryl, and nonarom. sulfoxides. The effect of pore size using naked silica was also studied, demonstrating that the pore size does not affect the resoln.

IT 763-95-1 824-86-2, Benzyl methyl sulfoxide 833-82-9, Benzyl phenyl sulfoxide 934-72-5, Methyl p-tolyl sulfoxide 948-56-1, Phenyl p-tolyl sulfoxide 951-92-8, p-Methoxyphenyl phenyl sulfoxide 1193-82-4, Methyl phenyl sulfoxide 1517-78-8, (-)-o-Tolyl p-tolyl sulfoxide 1519-39-7, (+)-Methyl p-tolyl sulfoxide 2169-00-8, Benzyl octyl sulfoxide 2843-91-6, (-)-Benzyl methyl sulfoxide 2844-08-8, (R)-Benzyl tert-butyl sulfoxide 2976-98-9, Butyl methyl sulfoxide 4170-71-2, Phenyl tert-butyl sulfoxide 4170-80-3, Ethyl phenyl sulfoxide 4820-07-9, (+)-Benzyl p-tolyl sulfoxide 4820-08-0, (S)-Benzyl p-tolyl sulfoxide 4850-71-9, (+)-Methyl phenyl sulfoxide 4850-72-0, (R)-Phenyl tert-butyl sulfoxide 5056-07-5, (-)-Methyl p-tolyl sulfoxide 7205-94-9, Chloromethyl phenyl sulfoxide 7417-77-8, (+)-p-Methylbenzyl p-tolyl sulfoxide 7417-81-4, (S)-Benzyl phenyl sulfoxide 10381-68-7, o-Tolyl p-tolyl sulfoxide 10381-70-1, Benzyl p-tolyl sulfoxide 14090-81-4, (+)-Benzyl methyl sulfoxide 14090-83-6, Phenylsulfinylacetic acid methyl ester 14094-11-2, Methyl tert-butyl sulfoxide 16487-10-8, 1,3-Dithiane 1-oxide 16491-20-6, (+)-Phenyl p-tolyl sulfoxide 18453-46-8, (-)-Methyl phenyl sulfoxide 20246-02-0, (R)-Benzyl phenyl sulfoxide 20288-52-2 20288-54-4, (S)-Benzyl tert-butyl sulfoxide 20451-53-0, Vinyl phenyl sulfoxide 20580-80-7, (R)-Methyl tert-butyl sulfoxide 20675-59-6, (S)-Phenyl p-tolyl sulfoxide 21865-07-6, Phenyl propyl sulfoxide 26756-22-9, Benzyl tert-butyl sulfoxide 33577-16-1 36293-57-9, Phenyl cyclohexanemethyl sulfoxide 40806-56-2, (S)-Methyl tert-butyl sulfoxide 42872-16-2, (+)-o-Tolyl p-tolyl sulfoxide 51207-25-1, (R)-Ethyl phenyl sulfoxide 51795-48-3, (R)-Butyl methyl sulfoxide 52147-67-8, Methylsulfinylacetic acid methyl ester 54234-79-6, (+)-Phenyl propyl sulfoxide 60301-03-3, (S)-o-Methoxyphenyl phenyl sulfoxide 60301-04-4, (R)-2-Methoxyphenyl phenyl sulfoxide 62076-10-2, (S)-Phenyl tert-butyl sulfoxide 63865-78-1, (S)-1,3-Dithiane 1-oxide 63865-79-2, (R)-1,3-Dithiane 1-oxide 79888-64-5, trans-2-Phenyl-1,3-dithiolane 1-oxide 79888-65-6, cis-2-Phenyl-1,3-dithiolane 1-oxide 89299-85-4, (S)-Vinyl phenyl sulfoxide 89299-86-5,

(R)-Vinyl phenyl sulfoxide 91902-74-8, 2-Methoxyphenyl phenyl sulfoxide 93974-18-6, 2-Phenyl-1,3-dithiane 1-oxide 95126-91-3, p-Methylbenzyl p-tolyl sulfoxide 95833-69-5 95833-70-8 98639-87-3, (R)-Chloromethyl phenyl sulfoxide 98639-89-5, (R)-Phenylsulfinylacetic acid methyl ester 103577-45-3, Lansoprazole 104113-36-2, (S)-Ethyl phenyl sulfoxide 106634-38-2, (S)-p-Methoxyphenyl phenyl sulfoxide 106634-39-3, (R)-p-Methoxyphenyl phenyl sulfoxide 109120-75-4, (-)-Phenyl propyl sulfoxide 113496-17-6, Ethyl 2-naphthyl sulfoxide 120965-00-6, (1R)-cis-2-Phenyl-1,3-dithiolane 1-oxide 120965-01-7, (1S)-cis-2-Phenyl-1,3-dithiolane 1-oxide 122331-46-8, (S)-Phenylsulfinylacetic acid methyl ester 132436-13-6, (1S)-trans-2-Phenyl-1,3-dithiolane 1-oxide 132436-14-7, (1R)-trans-2-Phenyl-1,3-dithiolane 1-oxide 138530-94-6, (+)-Lansoprazole **138530-95-7**, (-)-Lansoprazole 142235-66-3, (R)-1,3-Benzodithiole 1-oxide 142235-67-4, (S)-1,3-Benzodithiole 1-oxide 153782-37-7, 1,3-Benzodithiole 1-oxide 159280-43-0, (S)-Benzyl octyl sulfoxide 160998-20-9, (R)-Benzyl o-tolyl sulfoxide 160998-21-0, (S)-Benzyl o-tolyl sulfoxide 160998-22-1, Benzyl 2,4,6-trimethylphenyl sulfoxide 160998-24-3, (R)-Benzyl octyl sulfoxide 160998-25-4, (R)-p-Bromophenyl p-tolyl sulfoxide 160998-26-5, (S)-p-Bromophenyl p-tolyl sulfoxide 161104-27-4, (R)-Ethyl 2-naphthyl sulfoxide 161104-28-5, (S)-Ethyl 2-naphthyl sulfoxide 161104-29-6, (R)-Benzyl 2,4,6-trimethylphenyl sulfoxide 161104-30-9, (S)-Benzyl 2,4,6-trimethylphenyl sulfoxide 161104-35-4, (R)-p-Methylbenzyl phenyl sulfoxide 161104-36-5, (S)-p-Methylbenzyl phenyl sulfoxide 161104-37-6, Benzyl o-tolyl sulfoxide 161104-38-7, p-Bromophenyl p-tolyl sulfoxide 161249-13-4, (S)-p-Methylbenzyl p-tolyl sulfoxide 169332-19-8, p-Methylbenzyl phenyl sulfoxide 175850-40-5 175850-41-6 175850-42-7 175850-43-8 175850-44-9 176018-70-5, (S)-Chloromethyl phenyl sulfoxide 176018-71-6 176018-72-7
RL: ANT (Analyte); ANST (Analytical study)
(chiral sulfoxides enantiomeric resoln. by HPLC on amylose (S)-.alpha.-methylbenzyl carbamate phase coated on aminopropylated silica)

L3 ANSWER 24 OF 28 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:78726 CAPLUS
DOCUMENT NUMBER: 124:212226
TITLE: Direct HPLC separation of enantiomers of pantoprazole and other benzimidazole sulfoxides using cellulose-based chiral stationary phases in reversed-phase mode
AUTHOR(S): Tanaka, Makoto; Yamazaki, Hideki; Hakusui, Hideo
CORPORATE SOURCE: Dev. Res. Lab., Daiichi Pharm. Co. Ltd., Tokyo, Japan
SOURCE: Chirality (1995), 7(8), 612-15
CODEN: CHRLEP; ISSN: 0899-0042
PUBLISHER: Wiley-Liss
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A direct, isocratic, and simple reversed-phase HPLC method was described for the sepn. of enantiomers of the proton pump inhibitor, pantoprazole (PAN) by using cellulose-based chiral stationary phases (Chiralcel OD-R and Chiralcel OJ-R). Some structurally related chiral benzimidazole sulfoxides, rac-omeprazole (OME) and rac-lansoprazole (LAN), were also studied. Chiralcel OJ-R was successful in the resoln. of enantiomers of rac-PAN and rac-OME, while Chiralcel OD-R was most suitable for resolving the enantiomers of rac-LAN. Highest enantioselectivity to rac-PAN and rac-OME was achieved on Chiralcel OJ-R by using acetonitrile as an org. modifier, whereas methanol afforded better resoln. of rac-LAN on Chiralcel OD-R than acetonitrile. Increases in buffer concn. and column temp. decreased retention and did not improve the resoln. of the enantiomers on

both columns. Using a mixt. of 50 mM sodium perchlorate soln. and acetonitrile as a mobile phase at a flow rate 0.5 mL/min, max. sepn. factors of 1.26 and 1.13 were obtained for the enantiomers of rac-PAN and rac-OME using a Chiralcel OJ-R column, while max. sepn. factor of 1.16 was obtained for the enantiomers of rac-LAN using a Chiralcel OD-R column.

IT 73590-58-6, Omeprazole 102625-70-7, Pantoprazole 103577-45-3, Lansoprazole 119141-88-7, (-)-Omeprazole 119141-89-8, (+)-Omeprazole 138530-94-6, (+)-Lansoprazole **138530-95-7**, (-)-Lansoprazole 142678-35-1, (-)-Pantoprazole 142706-18-1, (+)-Pantoprazole
RL: ANT (Analyte); ANST (Analytical study)
(HPLC resoln. of pantoprazole and benzimidazole sulfoxides by using cellulose-based chiral stationary phases)

L3 ANSWER 25 OF 28 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:14311 CAPLUS
DOCUMENT NUMBER: 122:150538
TITLE: HPLC with carbohydrate carbamate chiral phases: influence of chiral phase structure on enantioselectivity
AUTHOR(S): Matlin, Stephen A.; Tiritan, Elizabeth M.; Crawford, Andrew J.; Cass, Quezia B.; Boyd, Derek
CORPORATE SOURCE: Dep. Chem., Univ. Warwick, Conentry, UK
SOURCE: Chirality (1994), 6(2), 135-40
CODEN: CHRLEP; ISSN: 0899-0042
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The enantioselective resoln. of trans-stilbene oxide and of 23 chiral sulfoxides was studied on cellulose and amylose tris(arylcarbamate) stationary phases coated on aminopropylated 7 .mu.m spherical silica with 500 .ANG. diam. pores. Cellulose tris-(3,5-dimethylphenylcarbamate) showed good resolving power for many of the sulfoxides and amylose tris(3,5-dimethoxyphenylcarbamate) showed advantages for the resoln. of certain sulfoxides which were not sepd. on other phases.

IT 824-86-2, (.+-.)-Methyl benzyl sulfoxide 833-82-9, (.+-.)-Phenyl benzyl sulfoxide 934-72-5, (.+-.)-Methyl p-tolyl sulfoxide 948-56-1, (.+-.)-Phenyl p-tolyl sulfoxide 951-92-8 1193-82-4, (.+-.)-Methyl phenyl sulfoxide 1439-07-2, (.+-.)-trans-Stilbene oxide 1517-78-8, (-)-o-Tolyl p-tolyl sulfoxide 1519-39-7, (+)-Methyl p-tolyl sulfoxide 2169-00-8, (.+-.)-Octyl benzyl sulfoxide 2843-91-6, (-)-Methyl benzyl sulfoxide 2976-98-9, (.+-.)-Methyl butyl sulfoxide 4850-71-9, (+)-Methyl phenyl sulfoxide 5056-07-5, (-)-Methyl p-tolyl sulfoxide 7417-77-8, (R)-4-Methylbenzyl p-tolyl sulfoxide 7417-81-4, (S)-Phenyl benzyl sulfoxide 10381-68-7, (.+-.)-o-Tolyl p-tolyl sulfoxide 14090-81-4, (+)-Methyl benzyl sulfoxide 14090-83-6 16487-10-8, (.+-.)-1,3-Dithiane 1-oxide 18453-46-8, (-)-Methyl phenyl sulfoxide 20246-02-0, (R)-Phenyl benzyl sulfoxide 20451-53-0, (.+-.)-Phenyl vinyl sulfoxide 25144-18-7, (+)-trans-Stilbene oxide 40102-60-1, (-)-trans-Stilbene oxide 42872-16-2, (+)-o-Tolyl p-tolyl sulfoxide 60349-76-0, (.+-.)-trans-2-Phenyl-1,3-dithiane 1-oxide 63865-78-1, (S)-1,3-Dithiane 1-oxide 63865-79-2, (R)-1,3-Dithiane 1-oxide 79888-64-5, (.+-.)-trans-2-Phenyl-1,3-dithiolane 1-oxide 79888-65-6, (.+-.)-cis-2-Phenyl-1,3-dithiolane 1-oxide 89299-85-4 89299-86-5 95126-91-3, (.+-.)-4-Methylbenzyl p-tolyl sulfoxide 98639-89-5 103577-45-3, (.+-.)-Lansoprazole 113496-17-6, (.+-.)-Ethyl 2-naphthyl sulfoxide 120965-00-6, (1R)-cis-2-Phenyl-1,3-dithiolane 1-oxide 120965-01-7, (1S)-cis-2-Phenyl-1,3-dithiolane 1-oxide 122331-46-8 131309-64-3, (1R)-trans-2-Phenyl-1,3-dithiane 1-oxide 132436-13-6, (1S)-trans-2-Phenyl-1,3-dithiolane 1-oxide 132436-14-7, (1R)-trans-2-Phenyl-1,3-dithiolane 1-oxide 138530-94-6, (+)-Lansoprazole **138530-95-7**, (-)-Lansoprazole 142235-66-3, (R)-1,3-Benzodithiole 1-oxide 142235-67-4, (S)-1,3-Benzodithiole 1-oxide 153782-37-7,

(.+-.)-1,3-Benzodithiole 1-oxide 159280-43-0, (S)-Octyl benzyl sulfoxide 159280-47-4, (.+-.)-Benzyl cyclohexyl sulfoxide 160496-18-4, (1S)-trans-2-Phenyl-1,3-dithiane 1-oxide 160998-20-9, (R)-Benzyl o-tolyl sulfoxide 160998-21-0, (S)-Benzyl o-tolyl sulfoxide 160998-22-1, (.+-.)-Benzyl mesityl sulfoxide 160998-24-3, (R)-Octyl benzyl sulfoxide 160998-25-4, (R)-p-Tolyl p-bromophenyl sulfoxide 160998-26-5, (S)-p-Tolyl p-bromophenyl sulfoxide 161104-27-4, (R)-Ethyl 2-naphthyl sulfoxide 161104-28-5, (S)-Ethyl 2-naphthyl sulfoxide 161104-29-6, (R)-Benzyl mesityl sulfoxide 161104-30-9, (S)-Benzyl mesityl sulfoxide 161104-33-2, (R)-Benzyl cyclohexyl sulfoxide 161104-34-3, (S)-Benzyl cyclohexyl sulfoxide 161104-35-4, (R)-Phenyl 4-methylbenzyl sulfoxide 161104-36-5, (S)-Phenyl 4-methylbenzyl sulfoxide 161104-37-6, (.+-.)-Benzyl o-tolyl sulfoxide 161104-38-7, (.+-.)-p-Tolyl p-bromophenyl sulfoxide 161249-13-4, (S)-4-Methylbenzyl p-tolyl sulfoxide 169332-19-8, (.+-.)-Phenyl 4-methylbenzyl sulfoxide
RL: ANT (Analyte); PRP (Properties); ANST (Analytical study)
(effect of chiral phase structure on enantioselectivity in HPLC with carbohydrate carbamate chiral phases)

L3 ANSWER 26 OF 28 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1994:491990 CAPLUS
DOCUMENT NUMBER: 121:91990
TITLE: Stereoselective effects in the separation of enantiomers of omeprazole and other substituted benzimidazoles on different chiral stationary phases
AUTHOR(S): Balmer, Karin; Persson, Bengt-Arne; Lagerstroem, Per-Olof
CORPORATE SOURCE: Bioanal. Chem., Moelndal, S-431 83, Swed.
SOURCE: Journal of Chromatography (1994), 660(1-2), 269-73
CODEN: JOCRAM; ISSN: 0021-9673
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The enantioselective sepn. of omeprazole on different chiral stationary phases was investigated. The two enantiomers could be resolved on three different phases with immobilized protein, Chiral-AGP, Ultron ES-OVM and BSA-DSC, employing aq. mobile phases with 2-propanol as org. modifier. On Chiralpak AD, an amylose-based chiral stationary phase, the enantiomers of omeprazole and three analogs could be sepd. using a non-polar hexane-ethanol mobile phase. For omeprazole the retention order was reversed when 2-propanol was replaced with ethanol or methanol as the modifier of hexane in the mobile phase.
IT 119141-88-7, (-)-Omeprazole 119141-89-8, (+)-Omeprazole 138530-94-6, (+)-Lansoprazole **138530-95-7**, (-)-Lansoprazole 142678-35-1, (-)-Pantoprazole 142706-18-1, (+)-Pantoprazole 154727-73-8 154727-74-9
RL: ANT (Analyte); ANST (Analytical study)
(sepn. of, by liq. chromatog., chiral stationary phases for)

L3 ANSWER 27 OF 28 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1992:490285 CAPLUS
DOCUMENT NUMBER: 117:90285
TITLE: Enantiomerically pure (pyridylmethylsulfinyl)benzimidazoles useful as drugs, and their preparation from racemates
INVENTOR(S): Kohl, Bernhard; Senn-Bilfinger, Joerg
PATENT ASSIGNEE(S): Byk Gulden Lomberg Chemische Fabrik GmbH, Germany
SOURCE: Ger. Offen., 8 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4035455	A1	19920514	DE 1990-4035455	19901108
WO 9208716	A1	19920529	WO 1991-EP2096	19911106
W: AU, CA, CS, DE, FI, HU, JP, KR, NO, PL, SU, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
AU 9188406	A1	19920611	AU 1991-88406	19911106

PRIORITY APPLN. INFO.: DE 1990-4035455 19901108
WO 1991-EP2096 19911106

OTHER SOURCE(S): MARPAT 117:90285

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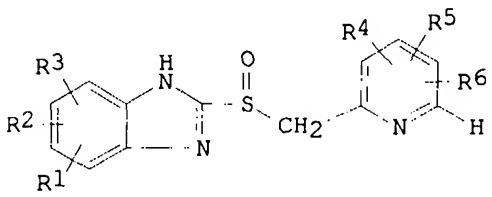

I

AB Title enantiomers I [R1, R5 = H, C1-4 alkyl, C1-4 alkoxy; R2 = H, CF3, alkyl, (fluorinated) alkoxy, ClCF2O, ClCHFCF2O; R3 = H, alkyl, (fluorinated) alkoxy, ClCF2O, ClCHFCF2O; or R2R3 = (fluorinated) C1-2 alkylenedioxy, OCFClCF2O; R4 = H, alkyl; R6 = (fluorinated) alkoxy, PhCH2O] and their salts, useful as drugs for gastric and intestinal disorders (no data), are prepd. by derivatizing their racemates (or racemate salts) at the benzimidazole N with an enantiomerically pure chiral compd., sepg. the resulting diastereomeric derivs., and solvolyzing the sepd. deriv. isomers in a strongly acidic medium. For example, (.+-.)-5-(difluoromethoxy)-2-[[(3,4-dimethoxy-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole Na salt [(.+-.)-II.Na] was N-alkylated by (+)-fenchyl chloromethyl ether [(+)-ROCH2Cl where R = fenchyl] in N-methylpyrrolidone to give a diastereomeric mixt. of (+)-II 1-(+)-CH2OR deriv. (III) and (-)-II 1-(+)-CH2OR deriv. in 74% yield. Four recrystns. from EtOAc/(iso-Pr)2O gave pure III (71.4% yield), which was hydrolyzed in 90% H2SO4 at 5-10.degree. with aq. NaOH workup and chromatog. to give 44% (+)-II, i.e. the (+)-isomer of pantoprazole. Addnl. examples show prepn. of (-)-II and of (+)-omeprazole.

IT 119141-88-7P, (-)-Omeprazole 119141-89-8P, (+)-Omeprazole
138530-94-6P, (+)-Lansoprazole **138530-95-7P**, (-)-Lansoprazole
142678-35-1P, (-)-Pantoprazole 142706-18-1P, (+)-Pantoprazole
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, by resoln. via fenchyloxymethyl deriv.)

L3 ANSWER 28 OF 28 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1992:51263 CAPLUS
DOCUMENT NUMBER: 116:51263
TITLE: Effects of the enantiomers of lansoprazole (AG-1749) on (hydrogen ion-potassium)-ATPase activity in canine gastric microsomes and acid formation in isolated canine parietal cells
AUTHOR(S): Nagaya, Hideaki; Inatomi, Nobuhiro; Nohara, Akira; Satoh, Hiroshi
CORPORATE SOURCE: Biol. Res. Lab., Takeda Chem. Ind. Ltd., Osaka, 532,

Japan
SOURCE: Biochemical Pharmacology (1991), 42(10), 1875-8
CODEN: BCPCA6; ISSN: 0006-2952
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of the enantiomers of lansoprazole on acid formation in isolated canine stomach parietal cells and (H+-K+)-ATPase activity in gastric microsomes were investigated. Both enantiomers of lansoprazole inhibited the acid formation stimulated by dibutyryl cAMP (db-cAMP) in a concn.-dependent manner with IC50 values of 59 and 82 nM, resp. The enantiomers showed concn.-dependent inhibition of (H+-K+)-ATPase with IC50 values of 4.2 and 5.2 .mu.M, resp. The IC50 values of lansoprazole for db-cAMP-stimulated acid formation and (H+-K+)-ATPase were 59 nM and 2.1 .mu.M, resp. The two enantiomers of lansoprazole have antisecretory action due to the inhibition of (H+-K+)-ATPase.
IT 138530-94-6 **138530-95-7**
RL: BIOL (Biological study)
(stomach ATPase and acid secretion response to, antiulcer activity in relation to)

=> file uspatall
FILE 'USPATFULL' ENTERED AT 16:18:58 ON 19 NOV 2003
CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPAT2' ENTERED AT 16:18:58 ON 19 NOV 2003
CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

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L2 1 SEA FILE=REGISTRY S(W)LANSOPRAZOLE
L4 6 SEA L2

=> d l4 1-6 ibib abs hit

L4 ANSWER 1 OF 6 USPATFULL on STN
ACCESSION NUMBER: 2003:245177 USPATFULL
TITLE: Process for producing optically active sulfoxide derivative
INVENTOR(S): Hashimoto, Hideo, Kobe-shi, JAPAN
Urai, Tadashi, Taktasuki-shi, JAPAN

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2003171591	A1	20030911	
APPLICATION INFO.:	US 2002-276109	A1	20021024	(10)
	WO 2001-JP3613		20010426	

	NUMBER	DATE
PRIORITY INFORMATION:	JP 2000-128760	20000428

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Mark Chao, Intellectual Property Department, Takeda Pharmaceuticals North America Inc, 475 Half Day Road Suite 500, Lincolnshire, IL, 60069
NUMBER OF CLAIMS: 11
EXEMPLARY CLAIM: 1
LINE COUNT: 1156
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to a production method of an optically

active form of a compound represented by formula (II) ##STR1##

wherein ring A is a benzene ring optionally having substituent(s); R.sup.1 is H, a hydrocarbon group optionally having substituent(s), an acyl group or an acyloxy group; R.sup.2, R.sup.3 and R.sup.4 are each H, an alkyl group optionally having substituent(s), an alkoxy group optionally having substituent(s) or an amino group optionally having substituent(s); X is N or CH; Y is N or CH; and * shows an asymmetric center, or a salt thereof, which includes reacting a compound represented by the formula (I) ##STR2##

wherein each symbol is as defined above, or a salt thereof, with an excess amount of an oxidizing agent in the presence of a catalyst for asymmetric induction, and provides an efficient production method of an optically active sulfoxide derivative in high yield on an industrial large scale by a convenient method, while achieving an extremely high enantiomer excess.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 73590-58-6P 103577-45-3P 138530-94-6P **138530-95-7P**
(process for producing optically active pyridylmethylsulfinylbenzimidazole derivs.)

L4 ANSWER 2 OF 6 USPATFULL on STN

ACCESSION NUMBER:	2003:222123 USPATFULL		
TITLE:	Crystals of benzimidazole compounds		
INVENTOR(S):	Fujishima, Akira, Sanda, JAPAN Aoki, Isao, Kawanishi, JAPAN Kamiyama, Keiji, Ibaraki, JAPAN		
PATENT ASSIGNEE(S):	Takeda Chemical Industries, Ltd., Osaka, JAPAN (non-U.S. corporation)		
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6608092	B1	20030819
	WO 2001002389		20010111
APPLICATION INFO.:	US 2001-19254		20011228 (10)
	WO 2000-JP4279		20000629
	NUMBER		DATE
PRIORITY INFORMATION:	JP 1999-186403		19990630
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	GRANTED		
PRIMARY EXAMINER:	Fan, Jane		
LEGAL REPRESENTATIVE:	Wenderoth, Lind & Ponack, L.L.P.		
NUMBER OF CLAIMS:	4		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	0 Drawing Figure(s); 0 Drawing Page(s)		
LINE COUNT:	601		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Crystals of (S)-2[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridinyl]methyl]sulfinyl]-1H-benzimidazole or salts thereof, useful as excellent antiulcer drugs.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **138530-95-7P** 318290-63-0P
(crystals of benzimidazole compds.)

L4 ANSWER 3 OF 6 USPATFULL on STN
ACCESSION NUMBER: 2003:220475 USPATFULL

TITLE: Process for producing crystal
INVENTOR(S): Hashimoto, Hideo, Hyogo, JAPAN
Maruyama, Hideaki, Osaka, JAPAN

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2003153766	A1	20030814	
APPLICATION INFO.:	US 2002-275334	A1	20021107	(10)
	WO 2001-JP4014		20010515	

	NUMBER	DATE
PRIORITY INFORMATION:	JP 2000-141670	20000515

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: TAKEDA PHARMACEUTICALS NORTH AMERICA, INC, INTELLECTUAL PROPERTY DEPARTMENT, 475 HALF DAY ROAD, SUITE 500, LINCOLNSHIRE, IL, 60069
NUMBER OF CLAIMS: 29
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 24 Drawing Page(s)
LINE COUNT: 1528
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to a production method of a crystal of (R)-2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methyl]sulfinyl]benzimidazole.n'H.sub.2O (wherein n' is about 0 to about 0.1) or a salt thereof, which characteristically includes crystallization from an organic solvent solution or suspension in which (R)-2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methyl]sulfinyl]-benzimidazole.nH.sub.2O (wherein n is about 0.1 to about 1.0) or a salt thereof has been dissolved or suspended, and the like, and provides a convenient method for efficiently producing an optically active sulfoxide derivative having an extremely high enantiomer excess in high yield at an industrial large scale.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 138530-94-6P **138530-95-7P**
(process for producing optically active [[[methyl(fluoroethoxy)pyridyl] methyl]sulfinyl]benzimidazole in specific crystal forms by crystn.)

L4 ANSWER 4 OF 6 USPATFULL on STN
ACCESSION NUMBER: 2001:165896 USPATFULL
TITLE: S-lansoprazole compositions and methods
INVENTOR(S): Barberich, Timothy J., Concord, MA, United States
Yelle, William E., Billerica, MA, United States
Rubin, Paul D., Sudbury, MA, United States

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2001025107	A1	20010927	
APPLICATION INFO.:	US 2001-854065	A1	20010511	(9)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1999-240262, filed on 29 Jan 1999, PENDING			

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-107460P	19981105 (60)
	US 1998-73141P	19980130 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: HESLIN & ROTHENBERG, PC, 5 COLUMBIA CIRCLE, ALBANY, NY,

12203
NUMBER OF CLAIMS: 12
EXEMPLARY CLAIM: 1
LINE COUNT: 469
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods and compositions are disclosed utilizing optically pure (-) lansoprazole for the treatment of ulcers in humans while substantially reducing the concomitant liability of adverse effects associated with the racemic mixture of lansoprazole. The optically pure (-) isomer is also useful for the treatment of gastroesophageal reflux. (-) Lansoprazole is an inhibitor of H.sup.+ release and is therefore useful in the treatment of other conditions related to gastric hypersecretion such as Zollinger-Ellison Syndrome.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **138530-95-7**, (-)-Lansoprazole
(oral compns. contg. optically pure S-lansoprazole)

L4 ANSWER 5 OF 6 USPATFULL on STN
ACCESSION NUMBER: 1999:106465 USPATFULL
TITLE: Process for synthesis of substituted sulphoxides
INVENTOR(S): Larsson, Magnus Erik, Bromma, Sweden
Stenhede, Urban Jan, Sodertalje, Sweden
Sorensen, Henrik, Molnlycke, Sweden
von Unge, Sverker Per Oskar, Fjar.ang.s, Sweden
Cotton, Hanna Kristina, .ANG.rsta, Sweden
PATENT ASSIGNEE(S): Astra Aktiebolag, Sodertalje, Sweden (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5948789		19990907	
	WO 9602535		19960201	
APPLICATION INFO.:	US 1995-492087		19950714	(8)
	WO 1995-SE818		19950703	
			19950714	PCT 371 date
			19950714	PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	SE 1994-2510	19940715

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Raymond, Richard L.
LEGAL REPRESENTATIVE: White & Case L.L.P.
NUMBER OF CLAIMS: 35
EXEMPLARY CLAIM: 1
LINE COUNT: 1521
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A novel process for enantioselective synthesis of single enantiomers of omeprazole or its alkaline salts, of other optically pure substituted 2-(2-pyridinylmethyl-sulphinyl) -1H-benzimidazoles as well as of other structurally related sulphoxides or their alkaline salts. The claimed process is an asymmetric oxidation of a pro-chiral sulphide to the single enantiomers or an enantiomerically enriched form of the corresponding sulphoxide. The application also claims the enantiomeric sulphoxide products produced by the process and their use in medicine.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 138530-94-6P **138530-95-7P** 142678-35-1P 142706-18-1P
154461-48-0P 156601-78-4P 156601-79-5P 170431-13-7P 170431-14-8P

175078-93-0P 177540-97-5P 177540-98-6P 177540-99-7P 177541-00-3P
177541-01-4P 177541-02-5P 177541-03-6P 177795-59-4P 177795-60-7P
177932-96-6P
(prepn. of unsym. heterocyclylsulfoxide enantiomers)

L4 ANSWER 6 OF 6 USPATFULL on STN

ACCESSION NUMBER:	1999:85595 USPATFULL		
TITLE:	Process for the optical purification of enantiomerically enriched benzimidazole derivatives		
INVENTOR(S):	Von Unge, Sverker, Fjar.ang.s, Sweden		
PATENT ASSIGNEE(S):	Astra Aktiebolag, Sodertalje, Sweden (non-U.S. corporation)		
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5929244		19990727
	WO 9702261		19970123
APPLICATION INFO.:	US 1996-676215		19960719 (8)
	WO 1996-SE841		19960626
			19960719 PCT 371 date
			19960719 PCT 102(e) date
	NUMBER		DATE
PRIORITY INFORMATION:	WO 1995-SE817		19950703
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Fan, Jane		
LEGAL REPRESENTATIVE:	White & Case L.L.P.		
NUMBER OF CLAIMS:	16		
EXEMPLARY CLAIM:	1		
LINE COUNT:	521		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Process for the optical purification of the single enantiomers of some 2-sulphinyl-1H-benzimidazole derivatives and another structurally related sulphoxide from the respective enantiomerically enriched preparation thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 119141-88-7P, (-)-Omeprazole 138530-94-6P, (+)-Lansoprazole
138530-95-7P, (-)-Lansoprazole 177541-00-3P, Benzenamine, 2-[(1H-benzimidazol-2-ylsulfinyl)methyl]-N-methyl-N-(2-methylpropyl)-, (-)- 177541-01-4P, Benzenamine, 2-[(1H-benzimidazol-2-ylsulfinyl)methyl]-N-methyl-N-(2-methylpropyl)-, (+)- 177795-59-4P
177795-60-7P 187589-30-6P
(optical purifn. of enantiomerically enriched 2-[(arylmethyl)sulfinyl]benzimidazole derivs.)